

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claims 1 to 30 (canceled)

Claim 31 (previously presented): A method for cleaving a nucleic acid substrate with a nucleic acid enzyme comprising mixing said substrate with the nucleic acid enzyme of claim 44.

Claims 32 to 43 (canceled)

Claim 44 (previously presented): A nucleic acid enzyme capable of recognizing and cleaving a nucleic acid substrate, said nucleic acid enzyme which when bound to the substrate comprises:

(i) a first nucleotide sequence

5'-G<sup>1</sup>G<sup>2</sup>G<sup>3</sup>U<sup>4</sup>C<sup>5</sup>C<sup>6</sup>A<sup>13</sup>C<sup>14</sup>C<sup>15</sup>UC<sup>16</sup>C<sup>17</sup>UCGCG<sup>15</sup>G<sup>14</sup>U<sup>13</sup>N<sup>1</sup>N<sup>2</sup>N<sup>3</sup>N<sup>4</sup>N<sup>5</sup>N<sup>6</sup>N<sup>7</sup>G<sup>17</sup>G<sup>16</sup>G<sup>7</sup>C<sup>8</sup>A<sup>9</sup>U<sup>10</sup>G<sup>11</sup>C<sup>12</sup>  
S<sup>1</sup>B<sup>1</sup>Y-3' (SEQ ID NO: 65); and

(ii) a second nucleotide sequence

5'-B<sup>2</sup>KS<sup>2</sup>G<sup>12</sup>C<sup>11</sup>A<sup>10</sup>U<sup>9</sup>G<sup>8</sup>G<sup>7</sup>CUAAGG<sup>6</sup>G<sup>5</sup>A<sup>4</sup>C<sup>3</sup>C<sup>2</sup>C<sup>1</sup>-3' (SEQ ID NO: 66);

wherein non-variable nucleotides having the same superscript form conventional Watson-Crick base pairs, except the two G<sup>7</sup> form a homopurine base pair;

S<sup>1</sup> and S<sup>2</sup> are each independently selected from the group consisting of G and C;

B<sup>1</sup> and B<sup>2</sup> are each independently selected from the group consisting of G, C, U and T;

K is selected from the group consisting of G, U and T;

Y is selected from the group consisting of C, U and T;

S<sup>1</sup> and S<sup>2</sup> form a conventional Watson-Crick base pair;

Y and B<sup>2</sup> may form a conventional Watson-Crick base pair;

B<sup>1</sup> and K may form a conventional Watson-Crick base pair;

B<sup>1</sup>, K, Y and B<sup>2</sup> may together form a loop;

N<sup>1</sup>N<sup>2</sup>N<sup>3</sup>N<sup>4</sup>N<sup>5</sup>N<sup>6</sup>N<sup>7</sup> forms a substrate binding region;

N<sup>1</sup>, N<sup>2</sup>, N<sup>3</sup>, N<sup>4</sup>, N<sup>5</sup> and N<sup>6</sup> are each a nucleotide which may be the same or different;

N<sup>7</sup> is U;

N<sup>7</sup> is capable of forming a wobble pair with the substrate;

N<sup>1</sup>, N<sup>2</sup>, N<sup>3</sup>, N<sup>5</sup> and N<sup>6</sup> are capable of forming conventional Watson-Crick base pairs with the substrate; and

N<sup>4</sup> is capable of forming a non-conventional Watson-Crick base pair and a conventional Watson-Crick base pair.

Claim 45 (previously presented): The nucleic acid enzyme of claim 44, wherein said enzyme comprises a nucleotide sequence selected from the group consisting of:

(i) 5'-G<sup>1</sup>G<sup>2</sup>G<sup>3</sup>U<sup>4</sup>C<sup>5</sup>C<sup>6</sup>A<sup>13</sup>C<sup>14</sup>C<sup>15</sup>UC<sup>16</sup>C<sup>17</sup>UCGCG<sup>15</sup>G<sup>14</sup>U<sup>13</sup>N<sup>1</sup>N<sup>2</sup>N<sup>3</sup>N<sup>4</sup>N<sup>5</sup>  
N<sup>6</sup>N<sup>7</sup>G<sup>17</sup>G<sup>16</sup>G<sup>7</sup>C<sup>8</sup>A<sup>9</sup>U<sup>10</sup>G<sup>11</sup>C<sup>12</sup>G<sup>18</sup>GCUUC<sup>18</sup>G<sup>12</sup>C<sup>11</sup>A<sup>10</sup>U<sup>9</sup>G<sup>8</sup>G<sup>7</sup>CUAAGG<sup>6</sup>G<sup>5</sup>A<sup>4</sup>C<sup>3</sup>C<sup>2</sup>C<sup>1</sup>-3',  
(SEQ ID NO: 61); and

(ii) 5'-G<sup>1</sup>G<sup>2</sup>G<sup>3</sup>U<sup>4</sup>C<sup>5</sup>C<sup>6</sup>A<sup>13</sup>C<sup>14</sup>C<sup>15</sup>UC<sup>16</sup>C<sup>17</sup>UCGCG<sup>15</sup>G<sup>14</sup>U<sup>13</sup>N<sup>1</sup>N<sup>2</sup>N<sup>3</sup>N<sup>4</sup>N<sup>5</sup>  
N<sup>6</sup>N<sup>7</sup>G<sup>17</sup>G<sup>16</sup>G<sup>7</sup>C<sup>8</sup>A<sup>9</sup>U<sup>10</sup>G<sup>11</sup>C<sup>12</sup>C<sup>18</sup>UUCGG<sup>18</sup>G<sup>12</sup>C<sup>11</sup>A<sup>10</sup>U<sup>9</sup>G<sup>8</sup>G<sup>7</sup>CUAAGG<sup>6</sup>G<sup>5</sup>A<sup>4</sup>C<sup>3</sup>C<sup>2</sup>C<sup>1</sup>-3',  
(SEQ ID NO: 62).

Claim 46 (previously presented): The nucleic acid enzyme of claim 44, wherein said first nucleotide sequence is

5'-G<sup>1</sup>G<sup>2</sup>G<sup>3</sup>U<sup>4</sup>C<sup>5</sup>C<sup>6</sup>A<sup>13</sup>C<sup>14</sup>C<sup>15</sup>UC<sup>16</sup>C<sup>17</sup>UCGCG<sup>15</sup>G<sup>14</sup>U<sup>13</sup>N<sup>1</sup>N<sup>2</sup>N<sup>3</sup>N<sup>4</sup>N<sup>5</sup>N<sup>6</sup>N<sup>7</sup>G<sup>17</sup>G<sup>16</sup>G<sup>7</sup>C<sup>8</sup>A<sup>9</sup>U<sup>10</sup>G<sup>11</sup>C<sup>12</sup>  
G<sup>18</sup>C<sup>19</sup>C<sup>20</sup>-3' (SEQ ID NO: 63) and said second nucleotide sequence is  
5'-G<sup>20</sup>G<sup>19</sup>C<sup>18</sup>G<sup>12</sup>C<sup>11</sup>A<sup>10</sup>U<sup>9</sup>G<sup>8</sup>G<sup>7</sup>CUAAGG<sup>6</sup>G<sup>5</sup>A<sup>4</sup>C<sup>3</sup>C<sup>2</sup>C<sup>1</sup>-3' (SEQ ID NO: 64).

Claim 47 (previously presented): The nucleic acid of claim 44, wherein  $N^1N^2N^3N^4N^5N^6N^7$  is selected from the group consisting of:

- (i) CCGACCU;
- (ii) CCCAGCU;
- (iii) GGGUAUUAU;
- (iv) CCGCCCCU;
- (v) CCGGCCU;
- (vi) CCGUCCU;
- (vii) CCGAACU;
- (viii) CCGAGCU;
- (ix) CCGAUCU;
- (x) CCUCUUU;
- (xi) CCUUGUU;
- (xii) UGUUCUU;
- (xiii) GGGGUUU;
- (xiv) UCCCCUU;
- (xv) GGACUCU;
- (xvi) UCGACUU; and
- (xvii) GCCACCU.

Claim 48 (previously presented): The nucleic acid enzyme of claim 44, wherein the enzyme is derived from hepatitis delta virus.

Claims 49 and 50 (canceled)

Claim 51 (previously presented): The nucleic acid enzyme of claim 44, wherein the enzyme is composed of ribonucleotides.

Claim 52 (previously presented): The nucleic acid enzyme of claim 44, wherein the enzyme is composed of a mixture of ribonucleotides and deoxyribonucleotides.

Claim 53 to 62 (canceled)

Claim 63 (new): A nucleic acid enzyme capable of recognizing and cleaving a nucleic acid substrate, said nucleic acid enzyme which when bound to the substrate comprises:

(i) a first nucleotide sequence

5'-G<sup>1</sup>G<sup>2</sup>G<sup>3</sup>U<sup>4</sup>C<sup>5</sup>C<sup>6</sup>A<sup>13</sup>C<sup>14</sup>C<sup>15</sup>UC<sup>16</sup>C<sup>17</sup>UCGCG<sup>15</sup>G<sup>14</sup>U<sup>13</sup>N<sup>1</sup>N<sup>2</sup>N<sup>3</sup>N<sup>4</sup>N<sup>5</sup>N<sup>6</sup>N<sup>7</sup>G<sup>17</sup>G<sup>16</sup>G<sup>7</sup>C<sup>8</sup>A<sup>9</sup>U<sup>10</sup>G<sup>11</sup>C<sup>12</sup>S<sup>1</sup>B<sup>1</sup>Y-3' (SEQ ID NO: 65); and

(ii) a second nucleotide sequence

5'-B<sup>2</sup>KS<sup>2</sup>G<sup>12</sup>C<sup>11</sup>A<sup>10</sup>U<sup>9</sup>G<sup>8</sup>G<sup>7</sup>CUAAGG<sup>6</sup>G<sup>5</sup>A<sup>4</sup>C<sup>3</sup>C<sup>2</sup>C<sup>1</sup>-3' (SEQ ID NO: 66);

wherein non-variable nucleotides having the same superscript form conventional Watson-Crick base pairs, except the two G<sup>7</sup> form a homopurine base pair;

S<sup>1</sup> and S<sup>2</sup> are each independently selected from the group consisting of G and C;

B<sup>1</sup> and B<sup>2</sup> are each independently selected from the group consisting of G, C, U and T;

K is selected from the group consisting of G, U and T;

Y is selected from the group consisting of C, U and T;

S<sup>1</sup> and S<sup>2</sup> form a conventional Watson-Crick base pair;

Y and B<sup>2</sup> may form a conventional Watson-Crick base pair;

B<sup>1</sup> and K may form a conventional Watson-Crick base pair;

B<sup>1</sup>, K, Y and B<sup>2</sup> may together form a loop;

N<sup>1</sup>N<sup>2</sup>N<sup>3</sup>N<sup>4</sup>N<sup>5</sup>N<sup>6</sup>N<sup>7</sup> forms a substrate binding region;

N<sup>1</sup>, N<sup>2</sup>, N<sup>3</sup>, N<sup>4</sup>, N<sup>5</sup> and N<sup>6</sup> are each a nucleotide which may be the same or different;

N<sup>7</sup> is U;

N<sup>7</sup> is capable of forming a wobble pair with the substrate;

N<sup>1</sup>, N<sup>2</sup>, N<sup>3</sup>, N<sup>5</sup> and N<sup>6</sup> are capable of forming conventional Watson-Crick base pairs with the substrate; and

N<sup>4</sup> is capable of forming a non-conventional Watson-Crick base pair and a conventional Watson-Crick base pair,

wherein the enzyme is incapable of forming a bond with the nucleotide residues of said substrate in positions -1 and -2 directly 5' to the cleavage site.

Claim 64 (new): The nucleic acid enzyme of claim 44, wherein G<sup>16</sup> and G<sup>17</sup> are incapable of forming a bond with the substrate.

Claim 65 (new): A nucleic acid enzyme capable of recognizing and cleaving a nucleic acid substrate, said nucleic acid enzyme which when bound to the substrate comprises:

(i) a first nucleotide sequence

5'-G<sup>1</sup>G<sup>2</sup>G<sup>3</sup>U<sup>4</sup>C<sup>5</sup>C<sup>6</sup>A<sup>13</sup>C<sup>14</sup>C<sup>15</sup>UC<sup>16</sup>C<sup>17</sup>UCGCG<sup>15</sup>G<sup>14</sup>U<sup>13</sup>N<sup>1</sup>N<sup>2</sup>N<sup>3</sup>N<sup>4</sup>N<sup>5</sup>N<sup>6</sup>N<sup>7</sup>G<sup>17</sup>G<sup>16</sup>G<sup>7</sup>C<sup>8</sup>A<sup>9</sup>U<sup>10</sup>G<sup>11</sup>C<sup>12</sup>S<sup>1</sup>B<sup>1</sup>Y-3' (SEQ ID NO: 65); and

(ii) a second nucleotide sequence

5'-B<sup>2</sup>KS<sup>2</sup>G<sup>12</sup>C<sup>11</sup>A<sup>10</sup>U<sup>9</sup>G<sup>8</sup>G<sup>7</sup>CUAAGG<sup>6</sup>G<sup>5</sup>A<sup>4</sup>C<sup>3</sup>C<sup>2</sup>C<sup>1</sup>-3' (SEQ ID NO: 66);

wherein non-variable nucleotides having the same superscript form conventional Watson-Crick base pairs, except the two  $G^7$  form a homopurine base pair;

$S^1$  and  $S^2$  are each independently selected from the group consisting of G and C;

$B^1$  and  $B^2$  are each independently selected from the group consisting of G, C, U and T;

K is selected from the group consisting of G, U and T;

Y is selected from the group consisting of C, U and T;

$S^1$  and  $S^2$  form a conventional Watson-Crick base pair;

Y and  $B^2$  may form a conventional Watson-Crick base pair;

$B^1$  and K may form a conventional Watson-Crick base pair;

$B^1$ , K, Y and  $B^2$  may together form a loop;

$N^1N^2N^3N^4N^5N^6N^7$  forms a substrate binding region;

$N^1$ ,  $N^2$ ,  $N^3$ ,  $N^4$ ,  $N^5$  and  $N^6$  are each a nucleotide which may be the same or different;

$N^7$  is U;

$N^7$  is capable of forming a wobble pair with the substrate;

$N^1$ ,  $N^2$ ,  $N^3$ ,  $N^5$  and  $N^6$  are capable of forming conventional Watson-Crick base pairs with the substrate; and

$N^4$  is capable of forming a non-conventional Watson-Crick base pair and a conventional Watson-Crick base pair,

wherein the enzyme is adapted to bind to the substrate such that the enzyme is incapable of interacting with nucleotide residues in the substrate at positions -1 and -2 directly 5' to the cleavage site and the enzyme is capable of forming a GU wobble pair with the nucleotide residue (G) in the substrate directly 3' to the cleavage site.